UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,474	09/25/2003	Douglas McNeel	011335.52703US	4831

23911 7590 01/12/2005

CROWELL & MORING LLP
INTELLECTUAL PROPERTY GROUP
P.O. BOX 14300
WASHINGTON, DC 20044-4300

EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,474	MCNEEL, DOUGLAS	
	Examiner	Art Unit	
	Louis D Lieto	1632	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *10-22,26,27 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,23-25,28-30 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the Restriction was received on 11/18/2004. Claims 1-32 are pending in the instant application. Applicant elected the subject matter of group I, drawn to a prostatic acid phosphatase (PAP) in a mammal comprising administering a recombinant DNA construct, with traverse. Original claims 10-22,26, 27, and 31 are withdrawn by the examiner from further consideration pursuant to 37 CFR 1.142(b). Claims 1-9, 23-25, 28-30, and 32 are currently under examination.

Election with Traverse

Applicant's election with traverse of group I, in the reply filed on 11/18/2004 is acknowledged. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the grounds of restriction for reasons of record as discussed below.

Applicant argues that the Examiner's restriction requirement between Groups I and II is deficient because the claim 10 is not distinct or independent from claim 1. Applicant points out that Independent claim 1 reads on a method comprising the administration of a polynucleotide encoding PAP to a mammal. Applicant further argues that independent claim 10 falls within the scope of claim 1 because even though it reads on the administration of two different polynucleotides encoding PAP's from different species it could have been re-drafted as a dependent claim from claim 1. Finally Applicant argues that these are not patentably distinct inventions; that they are merely related and should be rejoined. These arguments are not found persuasive:

As previously stated; the presence of an additional PAP construct from a different species makes the components and methodology of group II distinct from the invention of group I. Group I reads on a single PAP that can be structurally and functionally different from the PAP's of group II. Applicant's submitted sequence listing identifies 3 polynucleotides that encode PAP's; all of which differ in their coding sequences. Further, the PAP's from group II are required to be from different species, which means that the number of combinations of PAP's that can be administered to a mammal is N^2 versus N for group I. Group II reads on the induction of an immune reaction against PAP, which is interpreted to mean a single PAP because of the lack of plurality. This means that one of PAP's could be allogeneic and the second PAP an immunoreactive protein from a different species (see claim 11). The invention also encompasses, a non-immunoreactive, non-allogeneic PAP and a second PAP an immunoreactive protein from a different species. The subject matter that group II encompasses is substantially broader and has different elements than group I. While the inventions are related, in that they both read on the administration of PAP's, they read on different subject areas in the art, contain different elements, and will cause different biological responses. Further the inventions of groups I and II could be practiced separately since there is no requirement that the same PAP's be used in either invention. Finally, restriction practice based on independently claimed inventions is deemed proper when, as in the present application, they can be practiced separately. See MPEP § 808.01.

Applicant further argues that the examiner should rejoin groups I and II and cites portions of MPEP § 808.02. The examiner states that the inventions of groups I and II, despite having the same classification in the art and both reading on PAP, are distinct inventions with different fields of search. The classification of groups I and II is quite broad; different fields must be

searched because of the different subject matter encompassed by groups I and II, see above. Restriction is proper based on the requirement of searching different subject matter. See MPEP § 808.02(c).

Finally, applicant argues that because groups I &II and III & VI are related to each other as product and process for using the product they should be rejoined. This argument is not found persuasive.

Applicant is reminded that restriction is proper between a product and process for using if the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). See the prior action for specific arguments on the relevant differences. Since applicant did not specifically traverse the reasons stated in the previous office action in regards to the restriction between a product and process for using it is presumed that they are accepted and do not need to elaborated on. The requirement is still deemed proper and is therefore made FINAL.

Priority

Acknowledgment is made of applicant's claim for priority to Provisional Patent Application No. 60/413,777, filed 09/27/2002.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 23-25, 28-30, and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inducing a T cell or B cell mediated immune response to PAP in a mammal, comprising intramuscular, intravascular, intravenous, or intra-arterial administration of a recombinant pTVG or vaccinia virus construct comprising a polynucleotide sequence a PAP sequence linked to a promoter, does not reasonably provide enablement for a method for inducing any immune response to PAP in a mammal to treat prostate cancer, comprising any route of administration of any recombinant DNA construct comprising a polynucleotide sequence a PAP sequence linked to a any transcriptional regulatory element. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification teaches that administration of vector encoded PAP induces a cellular or humoral immune response. The responses observed are mediated by either T cells or B cells, which are considered to be components of the adaptive immune system. However, the specification dose not teach that vector encoded PAP can induce an innate immune response. The working examples only describe that vector encoded PAP can induce antibody production or cytotoxic T cell activity. The specification does not describe that NK cells, macrophages, mast cells, eosinophils or basophils are induced in response to vector encoded PAP. Further, the specification does not describe that PAP is capable of engaging any of the invariant receptors, such as the Toll, NKG2D, or CD94/NKG2E receptors, expressed on these cells and associated

with innate immune responses. Finally, the specification does not teach that vaccination with a DNA construct that encodes PAP can treat prostate cancer. The working examples show that PAP specific immune responses can be induced in rats after vaccination with DNA constructs encoding PAP; including PAP-specific cellular immunity, PAP-specific antibodies and autoimmune prostatitis. However, the specification does not describe any working examples in which DNA constructs that encode PAP were used to treat prostate cancer, either in humans or animal models. Rosenberg et al. teaches that plasmid DNA encoding "self" nonmutated tumor antigens were unable to immunize humans with metastasic melanoma *in vivo* {Rosenberg et al. (2003) Human Gene Therapy 14:709-714; Abstract; pg. 711, Table 1}. Thus Rosenberg et al. teaches that the efficacy of immunization with DNA constructs encoding "self" nonmutated tumor antigens remains unpredictable. Further, Hu et al teaches that vaccines can succeed in generating therapeutic T cells that recognize tumor antigens but that are ineffective in mediating tumor regression because of immune deviation {Hu et al. (1998) J. Immunol. 161:3033-3041; Abstract, pg. 3028, Table III}. Hu et al. teaches that some vaccine strategies may fail "as a result from the generation of an immune response that, while tumor-specific, does not lead to tumor regression" (pg. 3034, col. 1, pgph 1). Therefore, the art teaches that the successful treatment of a tumor is unpredictable based on the induction of an immune response against a tumor antigen by a vaccine.

The specification also does not provide an enabling disclosure for using any vector/promoter combination to express PAP *in vivo*, which causes the mammal to develop an immune reaction against PAP. The specification only discloses the use of a vaccinia virus and pTVFG constructs to express PAP *in vivo*. Verma et al. states that, the Achilles heel of gene

therapy is gene delivery, and that, most of the approaches suffer from poor efficiency of delivery and transient expression of the gene {Verma et al. (1997) Nature, Vol. 389, page 239, column 3, paragraph 2}. Marshall concurs, stating that, difficulties in getting genes transferred efficiently to target cells- and getting them expressed- remain a nagging problem for the entire field, and that, many problems must be solved before gene therapy will be useful for more than the rare application {Marshall (1995) Science, Vol. 269, page 1054, column 3, paragraph 2, and page 1055, column 1}. Orkin et al. further states in a report to the NIH that, none of the available vector systems is entirely satisfactory, and many of the perceived advantages of vector systems have not been experimentally validated, and that, while the expectations and the promise of gene therapy are great, clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol {Orkin et al. (1995) Report and recommendations of the panel to assess the NIH investment in research on gene therapy, page 1, paragraph 3, and page 8, paragraph 2}. Among the many factors that the art teaches affect efficient gene delivery and sustained gene expression are anti-viral immune responses, and the need for appropriate vector/promoter combinations for a particular cell type. In regards to the latter issue, Verma states that, the search for such combinations is a case of trail and error for a given cell type {Verma, (1997) Nature, 389, page 240}. Given the lack of guidance in the specification for any vector encoding to express PAP *in vivo*, which causes the mammal to develop an immune reaction against PAP, other than a vaccinia virus or a pTVG construct, a skilled artisan would be unable to practice the invention as claimed without arduous and extensive experimentation.

Finally, the specification fails to provide guidance on any method of administration of vector encoded PAP in order to induce an immune response. The specification only teaches

intramuscular, intravascular, intravenous, or intra-arterial vector administration (Specification pgph 60). However, the specification does not describe that administering the vector by oral or topical routes can induce any immune response. McCluskie et al. teaches that the route of delivery of DNA vaccine influences immune responses in laboratory animals {McCluskie et al. (1999) Mol. Med. 5:287-300; Abstract}. Specifically, in one study McCluskie et al. only observed antibody responses to injected routes of administration of DNA vaccines and not to non-injected injected routes of administration of DNA vaccines, such as oral routes, sub lingual, inhalation and vaginal wall (Abstract). The specification does not provide any working examples demonstrating that any route of application of vector encoded PAP is capable of inducing an immune response. Given the lack of guidance in the specification on how to induce any immune response in a mammal, the art taught unpredictability of immunization with DNA constructs encoding "self" non-mutated tumor antigens, the art taught unpredictability of correlating an immune response to a tumor antigen with a successful tumor treatment, the lack of teachings on how to administer any vector encoded PAP to induce any immune response, and the lack of teachings that an immune response can be induced by any route of vector administration, the skilled practitioner would be unable to practice the invention as claimed, except as a method for inducing an antigen specific immune response to PAP in a mammal, comprising intramuscular, intravascular, intravenous, or intra-arterial administration of a recombinant pTVG or vaccinia virus construct comprising a polynucleotide sequence a PAP sequence linked to a promoter, without arduous and extensive experimentation.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ...". (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 30 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 32. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 8, 9, 23-24, 28, 30, 32 rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6/328,969 (Dec. 11, 2001), hereafter referred to as Houghton et al.

Houghton et al. provides guidance on a method for inducing an immune response (pgph 1; claim 1) to prostatic acid phosphatase (PAP) (pgphs 3, 11 and 22) in a human (pgph 1) by administering a recombinant DNA construct comprising PAP (11), operatively linked to a promoter, such as CMV (pgph 21), to a human with prostate cancer (pgph 3). Further, Houghton et al. teaches the intramuscular administration of a recombinant DNA construct that encodes a human (pgph 3) or mouse (claim 6) PAP, and that a cytotoxic T cell response (pgph 26) and humoral immune response are induced against the PAP antigen (pgphs 3 and 6). Since Houghton et al was able to induce an immune response against the PAP antigen using a similar method any effects due to this immune response, such as destructive prostatitis, are inherently taught. Further, Houghton et al. teaches a vaccine in which the plasmid only expresses the PAP antigen (claim 1 and pgph 6); where the plasmid is delivered in a vaccine composition as a solution or suspension, in a lipid carrier, or by coating colloidal gold particles (pgph 6). Thus, by teaching all the limitations of the claims as written, Houghton et al. anticipates the instant invention as claimed.

Claims 25 and 29 are free of the prior art of the record.

No claims allowed.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy J Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information

Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Dr. Louis D. Lieto
Patent Examiner
Art Unit 1632

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER